High Dry Bean Intake and Reduced Risk of Advanced Colorectal Adenoma Recurrence among Participants in the Polyp Prevention Trial

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ABSTRACT Adequate fruit and vegetable intake was suggested to protect against colorectal cancer and colorectal adenomas; however, several recent prospective studies reported no association. We examined the association between fruits and vegetables and adenomatous polyp recurrence in the Polyp Prevention Trial (PPT). The PPT was a low-fat, high-fiber, high-fruit, and vegetable dietary intervention trial of adenoma recurrence, in which there were no differences in the rate of adenoma recurrence in participants in the intervention and control arms of the trial. In this analysis of the entire PPT trial–based cohort, multiple logistic regression analysis was used to estimate the odds ratio (OR) of advanced and nonadvanced adenoma recurrence within quartiles of baseline and change (baseline minus the mean over 3 y) in fruit and vegetable intake, after adjustment for age, total energyy intake, use of nonsteroidal anti-inflammatory drugs, BMI, and gender. There were no significant associations between nonadvanced adenoma recurrence and overall change in fruit and vegetable consumption; however, those in the highest quartile of change in dry bean intake (greatest increase) compared with those in the lowest had a significantly reduced OR for advanced adenoma recurrence (OR = 0.35; 95% CI, 0.18–0.69; *P* for trend = 0.001). The median in the highest quartile of change in dry bean intake was 370% higher than the baseline intake. The PPT trial–based cohort provides evidence that dry beans may be inversely associated with advanced adenoma recurrence. J. Nutr. 136: 1896–1903, 2006.

KEY WORDS: • *dry beans* • *fruits and vegetables* • *colorectal cancer* • *colorectal adenoma* • *advanced colorectal adenoma*

Colorectal cancer (CRC)[3] is the second leading cause of cancer death in the United States (1). Colorectal carcinoma (CRC) arises from neoplastic adenomatous polyps (2), and advanced adenomas, classified as either ≥1 cm in size, having ≥25% villous histology, or exhibiting high-grade dysplasia, are more likely to develop into colorectal cancer than smaller and lower-grade adenomas (3,4). Although the removal of adenomatous polyps at colonoscopy is thought to reduce colorectal mortality (5), the majority of Americans are unscreened (6). Therefore, studies that increase our understanding of modifiable risk factors for adenoma recurrence continue to be beneficial.

Several investigators reviewed the large number of studies on the effects of fruit and vegetable consumption and colorectal cancer risk (7,8). Although earlier and mostly case control studies showed protective associations with colorectal cancer, especially for vegetables, the majority of the more recent prospective studies found no associations (9). A recent meta-analysis that included both case-control and cohort studies found an overall weakly protective effect from vegetables and fruits for colorectal cancer (9). Most studies of adenomatous polyps reported that fruit and vegetable consumption is not associated with the risk of adenomas, although the risk estimates generally have been in the protective direction (10). To date, associations between colorectal adenomas and fruit intake were demonstrated in 1 case-control study (11) and 1 cohort study (12), whereas a protective association with

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[3] Abbreviations used: CRC, colorectal cancer; GI, glycemic index; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; PPT, Polyp Prevention Trial.

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vegetable intake was reported in a few case-control studies (13–16). A possible explanation for these equivocal findings is that some fruit and/or vegetable groups, but not all, are protective or that some may be more protective than others. Although associations between fruit and vegetable subgroups were investigated for colon and rectal cancer (17–19), the number of studies that have evaluated associations between fruit and vegetable subgroups with colorectal adenomas is limited (20).

The Polyp Prevention Trial (PPT), a multicenter randomized clinical trial, was designed to determine the effects of a high-fiber (4.30 g/MJ) high-fruit and -vegetable (5–8 servings/d), low-fat (20% of energy) diet on the recurrence of adenomatous polyps in the large bowel. Although the rate of adenoma recurrence did not differ between the intervention and control groups (21) after 4 y of intervention with all 3 goals targeted, the trial offered an opportunity to investigate further the effect of increasing fruits/vegetables and fruit and vegetable subgroups only on adenoma recurrence. The largest increase in fruit and vegetable intake was in dry beans, which tripled over the course of the intervention (22); therefore, this intervention trial offers a unique opportunity to investigate intake levels of dry beans not commonly observed in Western countries and the association with recurrence of adenomas. In this paper, we examined the relation between fruit, vegetables, dry beans, and other vegetable groups and colorectal adenoma recurrence in the PPT trial–based cohort, a population undergoing uniform colonoscopic surveillance.

SUBJECTS AND METHODS

Sample population. The overall design, rationale, dietary intervention and end point procedures, and trial results for the PPT were reported previously (21–24). Briefly, the study recruited 2079 men and women ≥35 y old between 1991 and 1994 at 8 clinical centers in the United States (listed in the Appendix). Participants had to have had 1 or more histologically confirmed colorectal adenomas identified by complete colonoscopy in the 6 mo before randomization. To be eligible, potential subjects must not have had prior surgically resected adenomatous polyps, or diagnoses with colorectal cancer, inflammatory bowel disease, or a polyposis syndrome. In addition, participants had to be ≤150% of their recommended weight and could not be currently using lipid-lowering medications. The study was approved by the Institutional Review Boards of the National Cancer Institute and each of the participating centers. All participants provided written informed consent at entry into the study.

At baseline and each of 4 annual follow-up visits, participants completed an interviewer-administered questionnaire including demographic, clinical, medication use, and dietary and supplement information and provided a blood sample after fasting for analysis of total cholesterol, carotenoids, and other biomarkers of interest. A baseline FFQ and 4-d food records were viewed before randomization to ensure that the participants' dietary patterns were not already similar to the intervention plan and to gauge the participants' ability to comply with recording dietary intake data (22). After randomization, intervention participants received instruction in the implementation of the PPT high-fiber, high-fruit and -vegetable, low-fat dietary plan; control participants received printed material on healthy eating, but no further information on diet from the study. A detailed description of the intervention and the dietary changes achieved was published previously (22). For the present study, 1905 participants who completed the full trial follow-up were evaluated.

Assessment of dietary intake and supplement use. Diet was assessed at baseline and annually with a modified Block-NCI FFQ Dietsys version 3.7 (25). Four-day records were collected for all subjects but only 20% were analyzed for comparison with the FFQ data. Before the collection of the dietary data, participants viewed instructional videos demonstrating food portion size estimates and received instruction in the completion of the dietary instruments. The FFQ queried usual food consumption patterns over the past year, and was used in the present analysis. The FFQ contained 11 questions on fruit consumption, 13 on vegetable consumption, and 3 on potato consumption. In this FFQ, a commonly used unit or portion of each food as eaten [such as 1 medium raw apple or one-half cup (~120 mL) of cooked spinach] was specified, and participants indicated how often, on average, they had consumed a small, medium, or large portion of that food over the past year. The frequencies were reported in 9 categories, ranging from <1 time/mo to ≥2 times/d. The following fruit and vegetable categories were examined: total fruits: all fruits, not including fruit juices; total vegetables: all individual vegetable questions including potatoes and dry beans; green leafy vegetables: spinach, mustard greens, collards, and turnip greens; cruciferous vegetables: broccoli, cauliflower, Brussels sprouts and cabbage; carrots, mixed vegetables containing carrots; starchy vegetables: corn, white potatoes, and sweet potatoes. A single question was asked about the intake of cooked dry beans, such as pinto, navy beans, lentils and bean soups. Intakes of green beans and green peas were queried separately. Food records (4-d) were used to assess the types of dry beans consumed. Participants were asked to bring all currently used prescription and nonprescription medications, including dietary supplements, to each annual visit, and information about the name, dosage, and frequency of use was recorded.

Assessment of adenomas. Participants received full colonoscopies at baseline, their 1-y visit, and at the end of the trial intervention, ~4 y after randomization. The colonoscopy at the 1st annual visit allowed for the detection and removal of any lesions missed by the baseline procedure. Pathologically confirmed adenomas diagnosed between the 1-y visit and the end of trial colonoscopy were considered recurrent adenomas. For participants who completed the baseline but missed the 1-y follow-up colonoscopy, recurrent adenomas were those detected at least 2 y after randomization. A total of 125 participants had an advanced adenoma recurrence and 629 participants had nonadvanced recurrent adenomas during follow-up. Biopsy samples of all adenomas removed during colonoscopy were reviewed independently by 2 pathologists to determine histological features and degree of atypia. Information on the size, number, and location of all lesions detected by colonoscopy was abstracted from endoscopy reports.

Statistical analyses. Statistical analyses were performed using Statistical Analysis Systems (SAS) software version 8.02. The characteristics of participants with and without recurrent adenomas (advanced and nonadvanced) were compared by t tests for continuous variables, and χ^2 test for categorical variables. For comparing change in fruit and vegetable variables by adenoma recurrence across 4 y of the trial, we conducted repeated measures of analysis using a linear mixed model. Specifically, we fit the linear mixed model with the outcome as the change from baseline in the repeated variables, fixed effects as adenoma recurrence (advanced vs. none and nonadvanced vs. none) and time effects, and a random intercept to account for between subject differences in the change across individuals. P-values were based on a log-likelihood test of an intervention effect (χ^2 with 1 df).

Odds ratios (ORs) and 95% CIs for the association between adenoma recurrence and dietary intake were estimated using logistic regression. Dietary variables were adjusted for total energy intake via the residual method of Willett and Stampfer (26). Data for dietary and supplement variables from all FFQs before the y-4 colonoscopy was used. Change in dietary intake was calculated as the difference between baseline intake and the mean of intake from all subsequent FFQs. Because the PPT was a dietary intervention trial, the baseline diet was likely different from follow-up, particularly for the intervention participants. To develop categorical variables, foods were grouped into quartiles based on distribution among the entire study population (1905) and were incorporated into models as indicator variables defined by the 2nd through 4th quartiles of intake, with the lowest quartile as the referent group. To conduct linear trend tests across levels of dietary intake, we created variables using exposure scores based on the median values for each quartile, and used these in logistic regression models. We evaluated the relation between dietary intake and either advanced adenoma recurrence or nonadvanced adenoma recurrence during the trial in logistic regression models. Our analyses compared those with an advanced adenoma recurrence (n = 125) to those with no recurrent adenoma (n = 1151), and those with nonadvanced adenoma (n = 629) to those with no recurrence (n =

1151). Potential confounders were evaluated by assessing their associations with both dietary variables and adenoma recurrence. Final models were adjusted for age, gender, total energy intake, BMI, and nonsteroidal anti-inflammatory drug (NSAID) use.

Effect modification by gender, intervention group assignment, and other covariates of interest was assessed by including the individual factor (e.g., gender) and its cross-product term with the continuous dietary variable in separate multivariate models for each potential effect modifier of interest. When significant meaningful interactions were observed, analyses were repeated, stratified at the median for the effect modifier. Last, to test for effect modification between baseline dry bean intake and change in dry bean intake on risk for advanced and nonadvanced adenoma recurrence, we created an interaction model with cross-product terms for baseline quartiles and change quartiles and compared the interaction model with a reduced model (without interactions terms) using a likelihood ratio ($\chi 2$) test with 9 df. Values are means ± SD. All statistical analyses were two-sided and differences were considered significant at $P < 0.05$.

RESULTS

Descriptive characteristics of study participants are presented in **Table 1**. The mean age among participants was 61.1 y and the mean BMI was 27.6 kg/m^2. A total of 64% of PPT participants were men, 90% were Caucasian, and >75% reported completing at least some education beyond high school. Approximately one-third of study participants reported baseline NSAID use, and 27% had a family history of colorectal cancer. Those with a nonadvanced recurrence were older and male, whereas those with advanced adenoma recurrence were older, male, and NSAID intake was less frequent.

For those with no recurrent adenomas, fruit and vegetable intake was 422.4.4 ± 195.6 g/d at baseline and increased by 172 ± 233.9 g/d over the 4 y of the trial (**Table 2**). Baseline intake of fruit, vegetables, or vegetable groups and the recurrence of advanced adenomas or nonadvanced adenomas did not differ. For those subjects with no recurrent adenomas, total vegetable intake (including dry beans) changed by 80.3 ± 131.8 g/d during the trial from a baseline level of 269.9 ± 125.2 g/d. Those with no recurrent adenomas increased their dry bean intake by 133%, which was the largest percentage change in any vegetable group. The change in intake of fruit, vegetables, or vegetable groups and the recurrence of nonadvanced adenomas did not differ. The change in level of total fruit and vegetable intake, and the change in vegetable intake between those with no adenoma recurrence and those with an advanced adenoma recurrence were both significant, $P = 0.01$, and $P = 0.006$, respectively. Change in intake of dry beans was significantly different in those with advanced adenomas ($P = 0.0007$) compared with those with no recurrent adenomas.

In multivariate logistic regression analyses, no significant associations existed between baseline dietary intake of total fruit and vegetable intake, fruits, vegetables, or vegetable groups; dry beans, peas and beans, cruciferous vegetables, starchy vegetables, white potatoes, dark green leafy vegetables, green salad, carrots and tomatoes and nonadvanced adenoma recurrence, or advanced adenoma recurrence, data not shown.

Because the intervention group made significant changes in their fruit and vegetable intake during the 4 y of the trial, we calculated the change (average minus baseline) in fruit and vegetable intake and evaluated the association between increased consumption and risk for recurrence in the entire study population. There were no significant associations between increased consumption of any of the fruit and vegetable variables, including dry beans, with the recurrence of nonadvanced colorectal adenomas (**Table 3**). However, the OR comparing the highest and lowest quartiles of change in dry bean intake showed a significant protective effect for the recurrence of advanced adenomas, OR = 0.35; 95% CI,0.18–0.69; P for trend = 0.001. Our findings for advanced recurrences were similar when the reference group was those with no adenomas or when the reference group included both those with no adenomas and those with any recurrence that was not advanced. All models were adjusted for age, gender, total energy intake, BMI, and NSAID use. An inverse association was also found between advanced adenomas and change in green bean and green pea intake, OR = 0.51; 95% CI, 0.28–0.92; P for trend = 0.01. Because individuals consuming high levels of dry beans might also consume high levels of green beans, we calculated the Spearman correlation coefficient between the change in intake in these 2 food groups in all participants in the advanced adenoma analysis ($n = 1241$). The correlation was moderate but significant, ($r = 0.32$; $P \leq 0.0001$). When both were entered into the same logistic regression model, risk estimates for green beans were attenuated and were no longer significant, whereas dry bean consumption continued to show a protective association with advanced adenoma recurrence after adjustment for green bean intake. Because red and processed meats are positively associated with colon cancer (27,28), and dry beans with their high protein content are often substituted in the diet for meat intake, we also adjusted for red meat or processed meat intake;

TABLE 1

Baseline characteristics of participants in the PPT-based cohort by adenoma recurrence[1,2]

Characteristic	Overall	No recurrence	Nonadvanced recurrence	Advanced recurrence	P-value nonadvanced[3]	P-value advanced[4]
Sample size, n	1905	1151	629	125	629/1151	125/1151
Age, y	61.1 (9.9)	59.9 (10.1)	62.3 (9.2)	60.8 (9.9)	<0.0001	<0.0001
BMI, kg/m^2	27.6 (3.9)	27.4 (4.0)	27.8 (3.8)	28.0 (4.1)	0.10	0.10
Male gender, %	64	60	72	70	0.0001	0.02
Caucasian, %	90	90	90	90	0.96	0.42
Education ≤high school, %	25	24	25	28	0.67	0.35
NSAID use, %	34	35	33	24	0.37	0.01
Family history of colorectal cancer, %	27	27	26	26	0.73	0.96

1 Values are means and SD for continuous variables and % for categorical variables, with P-values for differences in means determined by t test and differences in proportions determined by χ^2 test.

2 Adenomatous polyp recurrence and advanced adenoma recurrence diagnosed through postintervention at y 4.

3 Comparison between nonadvanced adenoma recurrence group to no adenoma recurrence group.

4 Comparison between advanced adenoma recurrence group to no adenoma recurrence group.

TABLE 2

Intake of fruits and vegetables among participants in the PPT-based cohort by adenoma recurrence[1–3]

Characteristic	No recurrence	Nonadvanced recurrence[4]	Advanced recurrence[5]	*P*-value nonadvanced	*P*-value advanced
Baseline T0[4]			*g/d*		
Sample size, *n*	1151	629	125	629/1151	125/1151
Fruits and vegetables	422.4 ± 195.6	433.9 ± 201.4	425.7 ± 209.5	0.24	0.86
Fruits	152.5 ± 115.3	160.3 ± 127.0	167.4 ± 125.5	0.20	0.18
Vegetables	269.9 ± 125.2	273.6 ± 119.9	258.3 ± 107.5	0.55	0.32
Dry beans	11.6 ± 16.2	11.6 ± 15.0	10.1 ± 15.6	0.93	0.14
Green beans and peas	18.5 ± 15.7	18.7 ± 15.8	16.3 ± 12.9	0.73	0.09
Cruciferous vegetables	24.5 ± 21.6	23.7 ± 26.7	23.8 ± 22.3	0.51	0.75
Starchy vegetables	55.0 ± 32.6	56.3 ± 31.8	53.6 ± 29.0	0.40	0.66
White potatoes	41.7 ± 28.2	42.9 ± 27.9	39.8 ± 25.3	0.40	0.47
Dark green leafy	7.4 ± 11.7	7.6 ± 14.1	7.7 ± 10.5	0.75	0.76
Green salad	41.2 ± 35.1	40.6 ± 34.9	40.8 ± 34.4	0.74	0.90
Carrots	14.1 ± 17.7	12.6 ± 15.5	12.1 ± 15.3	0.07	0.19
Tomatoes	28.7 ± 33.9	30.3 ± 35.5	27.9 ± 27.9	0.33	0.78
Change,[5] [(T1 + T2 + T3/3) − T0]			*g/d*		
Sample size	1120	613	121	613/1120	121/1120
Fruits and vegetables	172.2 ± 233.9	171.6 ± 230.7	134.9 ± 207.4	0.96	0.01
Fruits	91.9 ± 136.8	92.2 ± 138.7	57.6 ± 117.7	0.97	0.12
Vegetables	80.3 ± 131.8	79.4 ± 130.6	56.1 ± 115.7	0.89	0.006
Dry beans	15.4 ± 30.6	14.3 ± 28.8	8.4 ± 21.4	0.47	0.0007
Green beans and peas	5.8 ± 15.8	6.3 ± 17.2	3.8 ± 14.4	0.53	0.23
Cruciferous vegetables	8.0 ± 22.9	7.3 ± 24.5	7.0 ± 21.9	0.55	0.36
Starchy vegetables	5.7 ± 30.1	6.3 ± 31.6	3.8 ± 30.4	0.71	0.51
White potatoes	−0.3 ± 24.2	0.6 ± 25.7	0.9 ± 26.0	0.50	0.43
Dark green leafy	2.8 ± 11.4	2.8 ± 13.9	1.4 ± 9.3	0.92	0.21
Green salad	2.3 ± 28.3	3.4 ± 17.6	−1.4 ± 24.3	0.47	0.09
Carrots	5.0 ± 18.3	4.8 ± 17.6	3.5 ± 15.0	0.80	0.48
Tomatoes	2.7 ± 31.0	3.2 ± 32.9	5.5 ± 29.7	0.84	0.17

1 T0 values are means and SD with *P*-values for differences in means determined by *t* test.
2 Change values are means and SD with *P*-values for differences in change determined by repeated-measures ANOVA using a random effects mixed model.
3 Adenomatous polyp recurrence and advanced adenoma recurrence diagnosed through post-intervention at y 4.
4 Comparison between nonadvanced adenoma recurrence group, to no adenoma recurrence group.
5 Comparison between advanced adenoma recurrence group to no adenoma recurrence group.

however, neither adjustment changed the significant association for dry bean intake and advanced adenoma recurrence.

We also tested for an interaction between baseline dry bean intake and change in dry bean intake to assess whether baseline dry bean intake modified change in intake as it relates to recurrence. The interaction test was significant only for advanced recurrences ($\chi^2 = 17.47$, $P = 0.04$). At baseline, comparing the 4th quartile (median intake of dry beans 24.8 g/d) with the 1st quartile (0.72 g/d), there was no association with advanced adenoma recurrence, OR = 0.91; 95% CI, 0.15–1.06). Generally, the effects appeared to be strongest when individuals made a large change (4th quartile of change) from the lowest baseline quartile, suggesting a threshold effect well above the median 3rd quartile of change of 12 g/d.

Changes in fruit and vegetable intake were due mainly to increases made by participants in the intervention arm of the trial, whereas the control participants' fruit and vegetable intake remained close to baseline levels over the 4 y of the trial (22). For advanced adenoma recurrence, stratified by intervention group, there was a significant association with change in dry bean intake in the intervention group OR = 0.24; 95% CI,0.10–0.60; P for trend ≤ 0.0001. Because there were no control participants in the highest quartile of dry bean change, we repeated the analysis using tertile cut-offs for controls and found no significant association. For the recurrence of a nonadvanced adenoma stratified by group, the intervention OR comparing the highest quartile with the lowest quartile of change in dry bean intake tended to be reduced, but was not significant (OR = 0.67; 95% CI, 0.42–1.07).

In a separate analysis, we also examined whether the mean dry bean intake, from baseline through all dietary assessments before endpoint colonoscopy, was associated with advanced adenoma recurrence and found a very similar result. Comparing the 4th with the 1st quartile of average (T0 − T4) dry bean intake, OR = 0.30; 95% CI, 0.15–0.60; P for trend < 0.00001.

DISCUSSION

In the PPT, we observed a significant inverse association between increased dry bean consumption and the recurrence of advanced colorectal adenomatous polyps. Compared with subjects in the lowest quartile of change in intake of dry beans, participants in the highest quartile had a highly significant 65% reduction in the recurrence of advanced adenomas. There was also a 49% reduction in the recurrence of advanced adenomas

TABLE 3

Multivariate-adjusted OR and 95% CI for advanced and nonadvanced adenoma recurrence with mean change (baseline to the end of the trial) in consumption of fruits and vegetables among participants in the PPT (n = 1905)[1]

Quartile	Median	Cases	Nonadvanced recurrence OR (95% CI)	Cases	Advanced OR (95% CI)
		613		121	
Change, *g/d*					
Fruits and Vegetables					
1	−69.9	145	1.00	32	1.00
2	74.4	149	1.08 (0.81–1.44)	38	1.23 (0.74–2.06)
3	215.5	165	1.21 (0.91–1.67)	32	1.01 (0.59–1.71)
4	444.8	154	1.09 (0.82–146)	19	0.63 (0.34–1.15)
P for trend			0.54		0.09
Fruits					
1	−44.0	156	1.00	27	1.00
2	36.0	143	0.91 (0.69–1.22)	39	1.42 (0.84–2.42)
3	114.8	158	1.03 (0.78–1.37)	34	1.26 (0.73–2.17)
4	244.9	156	1.00 (0.75–1.32)	21	0.76 (0.41–1.39)
P for trend			0.83		0.23
Vegetables					
1	−59.2	146	1.00	38	1.00
2	31.6	161	1.17 (0.88–1.55)	32	0.91 (0.55–1.52)
3	106.1	152	1.06 (0.79–1.40)	29	0.78 (0.46–1.31)
4	223.4	154	1.09 (0.82–1.45)	22	0.63 (0.36–1.11)
P for trend			0.74		0.09
Dry beans					
1	−5.7	158	1.00	36	1.0
2	3.4	146	0.95 (0.71–1.27)	41	1.22 (0.74–2.00)
3	12.0	148	0.95 (0.71–1.26)	32	0.95 (0.56–1.60)
4	41.5	161	1.01 (0.76–1.34)	12	0.35 (0.18–0.69)
P for trend			0.82		0.001
Green beans and peas					
1	−8.5	157	1.00	37	1.00
2	1.6	144	0.89 (0.67–1.19)	41	1.08 (0.66–1.76)
3	8.1	152	0.92 (0.69–1.22)	25	0.72 (0.42–1.26)
4	21.6	160	1.00 (0.75–1.32)	18	0.51 (0.28–0.92)
P for trend			0.93		0.01
Cruciferous vegetables					
1	−10.4	151	1.00	24	1.00
2	1.7	155	1.03 (1.02–1.04)	39	1.55(0.90–2.69)
3	10.1	161	1.01 (0.76–1.35)	34	1.52(0.87–2.66)
4	27.2	147	1.10 (0.83–1.45)	24	1.02(0.56–1.86)
			0.75		0.89
Starchy vegetables					
1	−25.3	154	1.00	34	1.00
2	−1.7	141	1.03 (0.78–1.37)	30	0.80 (0.47–1.37)
3	13.8	160	1.16 (0.87–1.53)	28	0.92 (0.53–1.58)
4	37.2	158	1.02 (0.77–1.35)	29	0.83 (0.48–1.43)
P for trend			0.70		0.58
White potatoes					
1	−25.9	149	1.00	32	1.00
2	−4.5	158	1.14 (0.86–1.52)	28	0.85 (0.49–1.46)
3	7.3	151	1.06 (0.79–1.40)	26	0.87 (0.50–1.51)
4	23.9	155	1.07 (0.80–1.42)	35	1.15 (0.68–1.93)
P for trend			0.73		0.66
Dark green leafy					
1	−3.5	159	1.00	39	1.00
2	0.1	142	0.82 (0.62–1.10)	28	0.69 (0.41–1.16)
3	2.7	155	0.87 (0.65–1.15)	26	0.61 (0.35–1.05)
4	11.4	157	0.94 (0.71–1.25)	28	0.73 (0.43–1.23)
P for trend			0.99		0.30
Green salad					
1	−24.7	152	1.00	36	1.00
2	−3.0	146	0.95 (0.71–1.27)	37	0.96 (0.58–1.59)
3	8.3	148	0.94 (0.70–1.24)	28	0.72 (0.42–1.23)
4	27.6	167	1.14 (0.86–1.51)	20	0.58 (0.32–1.04)
P for trend			0.28		0.05

TABLE 3 (*continued*)

Multivariate-adjusted OR and 95% CI for advanced and nonadvanced adenoma recurrence with mean change (baseline to the end of the trial) in consumption of fruits and vegetables among participants in the PPT (n = 1905)[1]

Quartile	Median	Cases	Nonadvanced recurrence OR (95% CI)	Cases	Advanced OR (95% CI)
Carrots					
1	−7.9	152	1.00	31	1.00
2	1.0	149	0.95 (0.71–1.26)	24	0.70 (0.40–1.25)
3	6.9	161	1.13 (0.85–1.50)	32	1.06 (0.62–1.80)
4	19.9	151	1.07 (0.81–1.42)	34	1.23 (0.72–2.08)
P for trend			0.48		0.24
Tomatoes					
1	−23.7	146	1.00	35	1.00
2	−0.9	159	1.15 (0.86–1.53)	33	1.08 (0.64–1.81)
3	9.4	152	1.02 (0.71–1.36)	19	0.57 (0.32–1.04)
4	28.4	156	1.14 (0.85–1.52)	34	1.03 (0.62–1.65)
P for trend			0.47		0.64

[1] All models were adjusted for age, gender, total energy intake, BMI, and NSAID use.

comparing the lowest with the highest change in intake of green beans and peas. However, the correlation between the change in intake of dry beans and the change in green bean and peas was significant ($r = 0.32$ $P \leq 0.0001$); when both were entered into the same logistic regression model, the OR for green beans was attenuated and was no longer significant, whereas dry bean consumption continued to show a protective association with advanced adenoma recurrence after adjustment for green bean intake. This analysis of the PPT trial–based cohort is the first reported protective association between dry bean intake and advanced adenomatous polyp recurrence.

One of the difficulties in interpreting the relation between dry bean intake and colon cancer consumption from the current literature is that few studies examined dry beans as a separate category. Instead, many studies included a category for all legumes (18–20,29). Members of the Leguminosae family include dry beans, dry peas, green peas, green beans, lentils, soybeans, peanuts, and alfalfa (sprouts) (30), thus comprising a much wider variety of foods with diverse nutrient and phytochemical compositions.

We know of only one previous study that examined the association between bean intake as a separate food group and colorectal adenomas (15). This Japanese case-control study found a protective association between the intake of beans and adenomas, but did not describe the type of beans used in the study (15). Other adenoma studies that examined associations between legumes (20) or fiber from legumes (11,12,31) and adenomas found no association.

In the majority of recent large cohort studies, no associations were found between fruit and vegetable or legume consumption and the risk of colon and rectal cancer (9,18,19). In a cohort study of Seventh Day Adventists, comprised of both vegetarians and nonvegetarians, legume consumption was associated with a much lower relative risk of colon cancer (0.33 95% CI; 0.13–0.83), but only among those who ate red meat (32). In contrast, the majority of colorectal cancer case-control studies reported weak inverse associations with vegetable intake (7), and the results for legume consumption were more variable (33–37). Both Steinmetz (33) and Le Marchand (34) reported a protective association between legume intake and CRC in women, but not in men. Several groups of investigators found no associations between colon or rectal cancer and legumes (35–37). However, in 2 case-control studies that examined pulses (dry beans) as a separate category (38,39), a 50–60% reduction in colon cancer risk was shown.

The U.S. cohort studies, the Nurses Health Study (NHS) and the Health Professional Study (HPS) did not find any association between colon cancer and legume intake (18); in these same cohorts, however, dietary patterns characterized by high legumes, high fruit and vegetables, and low red meat were protective for colon cancer (40,41). Additionally, high dry bean consumption is part of the traditional Mediterranean diet, which was shown repeatedly to lower the risk of cancers of the large bowel, breast, and endometrium (42).

Most of the large cohort studies were conducted in Western countries with traditionally low dry bean intake. Unfortunately, few studies have provided quantitative data on dry bean intake. In a prospective cohort in the Netherlands, the mean intake of dry beans was only 4.9 g/d (19). Together with nuts and seeds, legumes provide only 2–4% of total energy intake in economically developed countries (43). For the entire PPT trial–based cohort, dry beans (cooked or canned) increased from11.8 ± 16.3 g/d to 31.8 ± 28.6 g/d, with a range in the upper quartile of intake between 31.0 and 233 g/d. Because dry beans counted as a fruit and vegetable serving, and are also rich sources of fiber and low in fat, their intake increased significantly in the PPT intervention group (27.6 ± 34.8 g/d) compared with the control group (1.4 ± 15.2 g/d). The total intake of dry beans in the intervention group was ~39 g/d, which is considerably higher than the usual intake for U.S. men (21 g/d) and women (13 g/d) ≥60 y old (44). The association between advanced adenoma recurrence and dry bean intake appears to be a threshold effect that occurs well above the 3rd quartile of change, a level much higher than usually consumed in Western countries. This type of threshold effect is observed frequently in nutritional epidemiology; for example, Slattery reported a threshold effect of 5 servings/d of vegetables for reduction in the risk of rectal cancer (45). Using 4-d food records in a random subset of participants ($n = 455$), we examined the type of dry beans consumed by PPT participants. The 5 most highly consumed type of dry beans, in descending order, were baked beans, kidney beans, pinto beans, lima beans, and navy beans.

Although most colorectal carcinomas are thought to arise from colorectal adenomas (46,47), most adenomas, which are quite common, do not progress to the invasive carcinoma stage (48,49). It is generally assumed that advanced adenomas are more likely to progress to cancer than small tubular adenomas (3). Smith-Warner (20) suggested that because increased vegetable consumption is associated more strongly with a lower risk of colorectal cancer than adenomas, vegetables may have a stronger role in preventing the progression of adenomas to carcinomas rather than in preventing the initial appearance of adenomas. The finding in the PPT for the reduction in advanced adenoma recurrence with high dry bean intake supports this hypothesis.

Dry beans contain a wide range of nutrients and nonnutrient bioactive constituents that may be protective against cancer (43,50). The nondigestible carbohydrates are all fermented by colonic microflora into butyrate, a short-chain fatty acid, with demonstrated antineoplastic (51) and anti-inflammatory actions (52,53). Furthermore, dry beans have a low glycemic index (GI), defined as the incremental area under the blood glucose curve induced by a specific carbohydrate-containing food (54), which reduces the rate of the absorption of carbohydrates and lowers the postprandial glycemic and insulinemic responses. A number of epidemiologic studies showed that a low-GI diet is associated with a reduced risk of CRC (55–57). Other bioactive constituents of dry beans that have anticarcinogenic properties and could potentially account for a protective effect include saponins, protease inhibitors, inositol hexaphosphate, γ-tocopherol, and phytosterols (49). It is also possible that the combination of several different constituents of dry beans is most effective in reducing cancer risk.

The strengths of this study include the prospective design, the use of multiple measures dietary intake, and the large sample size. By using dietary intake over 4 time points rather than having only 1 measurement, intraindividual variation in exposure is attenuated, resulting in a more precise estimate of effect. Finally, because this intervention emphasized dry beans, the level of intake far exceeds that commonly consumed in the U.S and other Western countries. The short duration of adenoma recurrence trials, usually $<$4 y, has been used to explain the mostly null results observed from dietary intervention trials (21,58,59). Yet, during similarly short time frames, targeted single-agent interventions such as calcium supplement or aspirin intervention were shown to reduce the recurrence of adenomas compared with a placebo (60,61). In our current analysis, the repeated FFQs provided the opportunity to examine the effect of changes in intake of selected aspects of the PPT, in this case, specific vegetables such as dry beans, across the 4 y of the trial. There was a significant effect due to change in dry bean intake, suggesting that a short-term intervention with dry beans could also be effective in reducing advanced colorectal adenomas.

There are a number of limitations to our study. Individual volunteers for the PPT were relatively healthy nonsmokers, thereby limiting the generalizability of the findings to similar populations. As is well appreciated in the literature, all self-report dietary instruments are subject to measurement error, both random and systematic (26). Because participants in the intervention group knew exactly what was required of them, it is possible that they misreported true dietary intake of fruit and vegetables. Moreover, PPT study participants were not assigned randomly to a dry bean intervention. Additionally, intervention group participants made numerous dietary changes by lowering fat, increasing fiber, and increasing fruits and vegetables, which could result in residual or unmeasured confounding. Finally, these results should be interpreted cautiously given that they may have arisen by chance in the course of examining multiple associations. Nevertheless, our results suggest that a high level of dry bean intake reduces the recurrence of advanced adenoma recurrence. These findings must be replicated in other prospective studies of adenoma recurrence, and future studies investigating potential chemopreventive properties of dry beans should be undertaken.

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APPENDIX

The members of the Polyp Prevention Study Group participated in the conduct of the Polyp Prevention Trial. However, the data presented in this manuscript and the conclusions drawn from them are solely the responsibility of the co-authors of this paper.

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